REMARKS

Reconsideration and withdrawal of the rejections of the claimed invention is respectfully requested in view of the amendments, remarks and enclosures herewith, which place the application in condition for allowance.

I. STATUS OF SPECIFICATION, CLAIMS AND FORMAL MATTERS

The amendment to the specification was made to insert text which was inadvertently omitted from the filing of the present application. The portion of the specification deleted, i.e. page 3, lines 27-34, has been recopied in the amendment up to the phrase "...makes no contribution to the release of..." (see line 7 of the above amendment). The additional text added corresponds to the text from the provisional application upon which this application claims priority (see page 3, line 28 thru page 4, line 27 of Provisional SN: 60/462,630).

Claims 1-20 are still pending in this application. Claim 1 has been amended to add the limitations of original claims 4, 10 and 11. No new matter has been added by this amendment. The applicants reserve the right to pursue the scope of the originally filed claims in a continuation application.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. THE OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION HAS BEEN OVERCOME

Claims 1-20 have been provisionally rejected under obviousness-type double patenting over claims 1-28 of copending Application No. 10/835,997 in view of US 6,348,501. It is noted that the scope of the active substances in the '997 application has been limited to estradiol hemihydrate, bupranolol and testosterone in the preliminary amendment which was filed on 15 February 2008 and the scope of the active substances in the present case has been limited to capsaicin and analogs thereof. As such, the double-patenting rejection has been rendered moot.

III. THE 35 U.S.C. 112, 2nd PARAGRAPH REJECTION HAS BEEN OVERCOME

Claims 1-20 were rejected as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. The applicants request reconsideration of this rejection for the following reasons.

Claim 1 has been amended to remove the range within a range language. With regard to the phrase "saturation concentration", this term is well recognized in the art and would be determinable by those of ordinary skill in the art; saturation is known to describe the state of a solution when it hold the maximum equilibrium quantity of dissolved matter, i.e. being in excess of this equilibrium would cause the dissolved matter to precipitate out of solution. Here, the applicants are defining that the amount of the therapeutic compound in relation to the saturation concentration.

Claim 4 has been amended to remove the phrase "such as", however, it is noted that double inclusion is not automatically indefinite.[1] (The limitation of original claim 4 has been inserted into claim 1)

With regard to the description "medium tack" and "high tack" in claim 11 (now as applicable to claim 1), the specification does provide a means for one of ordinary skill in the art to determine the meaning and scope of the claim. See, e.g., page 5, lines 12-15 of the specification: "The high tack version used in the examples is tacky enough to stick on human skin. The medium tack version is nearly not tacky at all but is useful to compensate the softening effect of other ingredients like, e.g., in this case capsaicin and the solvent of microreservoirs."[2] In addition, the applicants show product literature from Dow Corning

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[1] "Similarly, the double inclusion of an element by members of a Markush group is not, in itself, sufficient basis for objection to or rejection of claims. Rather, the facts in each case must be evaluated to determine whether or not the multiple inclusion of one or more elements in a claim renders that claim indefinite. The mere fact that a compound may be embraced by more than one member of a Markush group recited in the claim does not necessarily render the scope of the claim unclear. For example, the Markush group, 'selected from the group consisting of amino, halogen, nitro, chloro and alkyl" should be acceptable even though 'halogen' is generic to 'chloro.'" *See MPEP 2173.05(h), Section I.*

[2] The examiner's focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, ***not whether more suitable language or modes of expression are available.*** When the examiner is satisfied that patentable subject matter is disclosed, and it is apparent to the examiner that the claims are directed to such patentable subject matter, he or she should allow claims which define with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire. ***Examiners are encouraged to suggest claim language to applicants to improve clarity or precision of the language used, but should not reject claims or insist on their own preferences if other modes of expression selected by applicants satisfy the statutory requirement.*** *See MPEP 2173.02.*

Healthcare which shows that the reference to medium and high tack is understandable to those of ordinary skill in the art.

Claims 9, 13 and 14 have been amended to remove the "preferably" language.

IV. THE 35 U.S.C. 101 REJECTION HAS BEEN OVERCOME

Claims 17-19 were rejected. The applicants request reconsideration of this rejection in light of the amendments made to claims 17-19.

V. THE 35 U.S.C. 103(a) REJECTION HAS BEEN OVERCOME

Claims 1-11, 13-14 and 17-20 were rejected as allegedly being obvious by Oloff et al. (US 5,071,657 – "Oloff") in view of Holt et al. (US 6,348,501 – "Holt"). The applicants request reconsideration of this rejection for the following reasons.

In order to establish a holding of *prima facie* obviousness, each of the applicants claim limitations must be taught or suggest by the prior art and if the combinations of limitations are found in more than one reference, there must be some reason either within the prior art or from the knowledge from those of ordinary skill in the art to combine the respective teachings. However, there are several differences between the applicants' claims and the combination of Oloff and Holt.

First, the Oloff reference while generally directed toward the delivery of an active agent is primarily directed toward the delivery of a steroid hormone. No mention of capsaicin is made anywhere in the Oloff reference.

Second, in the Oloff reference, the active agent is dissolved in a *nonflowable gel that form microdispersions*. The Office Action states "microdispersions (microreservoirs)" as though these are equivalent terms. This is erroneous. A microdispersion is a two-phase system with finely divided particles distributed through a bulk system. The active agent of the applicants' invention is not a particle but is dissolved in the microreservoir.

In order to maximize the benefit of the treatment of neuropathic pain, it is preferred to have a high concentration of capsaicin or a capsaicin analog being delivered at the application site. Achieving this high concentration is predicated on avoiding having the capsaicin or a capsaicin analog in solid form as is disclosed in the Oloff reference. The applicants have

achieved this via the use of the microreservoirs. In addition, after the capsaicin or a capsaicin analog has been dissolved, it is desired to avoid formation of solid capsaicin or a capsaicin analog by recrystallization. This is achieved in the applicants' invention by maintaining the concentration of the capsaicin or a capsaicin analog at 20 and 90% by weight of the saturation concentration. Nothing in the Oloff reference (or the Holt reference) teaches this aspect of the applicants' invention.

Third, the Examiner refers to col. 3, lines 55-67 as being a teaching for amine resistant polysiloxanes. However, this is also erroneous as none of the polysiloxanes have the free silanol groups derivatized with a trialkylsilyl group (e.g. trimethylsilyl) or other derivations which provide amine resistance.

The Holt reference does not remedy the deficiencies of Oloff and does not refer to an analogous invention to Oloff which would suggest to one ordinary skill in the art that individual elements of Holt could be used with Oloff.

Holt does teach the use of capsaicin. However, it is part of a lotion (a suspension or dispersion) where the capsaicin is encapsulated by an encapsulation agent. This is neither the mechanism of delivery of the active agent for either the applicants' invention or for Oloff. While the applicant's invention (topical patch) and Oloff (device for transdermal administration) are directed toward controlled release of an active agent, Holt's lotion has no such control and as such one of ordinary skill in the art would not look to Holt's teachings as being relevant for the applicants' invention or that of Oloff. Even if it were permissible to combine Holt with Oloff, the combined teachings would still lack a teaching of the use of microreservoirs and that the active agents are dissolved therein and that the concentration of capsaicin or a capsaicin analog is at 20 and 90% by weight of the saturation concentration.

Additionally, Holt does not remedy Oloff's omission of teaching an amine resistant polysiloxane.

For these reasons, the combination of Oloff and Holt does not render the applicants' claimed invention to be obvious as all claim limitations are not taught.

Claim 12 was rejected as allegedly being obvious by US 5,071,657 in view of US 6,348,501 and in further view of Brown et al. (US 7,247,315 – "Brown"). The applicants request reconsideration of this rejection for the following reasons.

The applicants' arguments with respect to the combination of Oloff and Holt is considered to be repeated here. Brown does not remedy the deficiencies of the combination of Oloff and Holt and is not even appropriate for its intended use to support the rejection of claim 12, i.e. one of the procedures for determining a *prima facie* case of obviousness is to consider the applicants' invention as a whole and also the references of interest as a whole.

There is simply no reason why one of ordinary skill in the art (who does not possess a copy of the applicants' claims to act as a blueprint) would be specifically directed toward silicone oil in Brown to the exclusion of all other possible teachings within the Brown reference. This is especially true in this case as Brown is directed toward yet another means of delivery for yet another type active agent (fentanyl or sufentanyl in Brown) which is different from Oloff and Holt's delivery methods, i.e. Brown is directed toward the delivery of the active ingredient from a solid drug reservoir which differs from the microdispersions of Oloff and encapsulating agents of Holt. There would be no expectation of success that taking an individual element from Brown would not change the function of either Oloff or Holt's invention alone or in combination.

Claims 15 and 16 were rejected as allegedly being obvious by US 5,071,657 in view of US 6,348,501 and further in view of Peterson (US 5,494,680). The applicants request reconsideration of this rejection for the following reasons.

The applicants' arguments with respect to the combination of Oloff and Holt is considered to be repeated here. Peterson does not remedy the deficiencies of the combination of Oloff and Holt and similar to the objection of the use of Brown above, Peterson is being used for specific elements to the exclusion of considering the invention as a whole, i.e. Peterson also is directed to a different delivery system than Oloff and Holt and also a different active agent than Oloff and Holt and there is no reason to pick specific elements from Peterson to the exclusion of their other teachings.

Claims 17-19 were rejected as allegedly being obvious by US 5,071,657 in view of US 6,348,501 and further in view of Robbins (US 6,239,180). The applicants request reconsideration of this rejection for the following reasons.

Robbins does refer to a method of treating neuropathic pain with capsaicin, but does not teach the topical patch of the applicants' invention for the reasons cited above with respect to Oloff and Holt.

Rejections using US 2004-0202710

Preliminary note:

The applicants wish to inform the Examiner that US 2004/0202710 is ineligible for use as prior art against the present invention because it ***DOES NOT*** qualify as prior art under 102(e), i.e. the '710 publication is not filed by another.[3] Both the '710 publication and the present invention have only a single inventor, Dr. Walter Müller.

However, the '710 publication is a continuation of SN: 10/019,378 which in turn is a National Stage application of PCT/EP00/05658. The PCT application was published as WO 01/01967 on 11 January 2001. This PCT publication ***DOES*** qualify as prior art under 35 U.S.C. 102 and therefore, the rejection should have been made over this publication although for the reasons cited below, the applicants explain that this reference does not render the present application to be obvious.

Claims 1-11 and 13-20 were rejected as allegedly being obvious over US 2004/0202710 ("the '710 publication") in view of Holt et al. (US 6,348,501 – "Holt"). The applicants request reconsideration of this rejection for the following reasons.

The rejection appears to acknowledge that the '710 publication does not teach a topical patch which contains capsaicin. However, merely finding a reference which refers to capsaicin is not sufficient to support a *prima facie* holding of obviousness; there must be a reasonable expectation of success for the substitution.

The transdermal therapeutic system of the '710 publication also uses microreservoirs to dissolve the active ingredient and the scope of the active agents for the claims under prosecution in the '710 publication (SN: 10/835,997) have been limited in response to the Examiner's rejection based on the scope of the active agents (Examiner for this application is also the same examiner for the '997 application) and as such it is incongruous to hold that the broad scope of

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[3] (e) the invention was described in - (1) an application for patent, published under section 122(b), **by another** filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language; or

active agents (including the classes of compounds recited in the specification) is rejected for the '997 application, but is supportive for a compound, i.e. capsaicin, which is not even mentioned in the '997 application.

For the reasons cited above, Holt does not provide further guidance for the necessary substitution. Holt is part of a lotion (a suspension or dispersion) where the capsaicin is encapsulated by an encapsulation agent. This is neither the mechanism of delivery of the active agent for either the applicants' invention or for the '710 publication. While the applicant's invention (topical patch) and the '710 publication (transdermal therapeutic system) are directed toward controlled release of an active agent, Holt's lotion has no such control and as such one of ordinary skill in the art would not look to Holt's teachings as being relevant for the applicants' invention or that of the '710 publication.

In addition, neither the '710 publication nor Holt refer to having capsaicin or a capsaicin analog which is in a concentration of 20 and 90% by weight of the saturation concentration.

Claim 12 was rejected as allegedly being obvious by US 2004/0202710 and US 6,348,501 and in further view of US 7,247,315. The applicants request reconsideration of this rejection for the following reasons.

The applicants' arguments with respect to the '710 publication is considered to be repeated here. Brown is not appropriate for its intended use to support the rejection of claim 12, i.e. one of the procedures for determining a *prima facie* case of obviousness is to consider the applicants' invention as a whole and also the references of interest as a whole.

There is simply no reason why one of ordinary skill in the art (who does not possess a copy of the applicants' claims to act as a blueprint) would be specifically directed toward silicone oil in Brown to the exclusion of all other possible teachings within the Brown reference. This is especially true in this case as Brown is directed toward another means of delivery for another type active agent (fentanyl or sufentanyl in Brown) which is different from the delivery method and active agent of the '710 publication.

Claims 17-19 were rejected as allegedly being obvious by US 2004/0202710 and US 6,348,501 and further in view of US 6,239,680. The applicants request reconsideration of this rejection for the following reasons.

Robbins does refer to a method of treating neuropathic pain with capsaicin, but does not teach the topical patch of the applicants' invention for the reasons cited above with respect to the '710 publication.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,
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Enclosure: "Silicone Adhesives" – product literature from Dow Corning Healthcare Selection Guide

Silicone Adhesives

To assure consistent quality for pharmaceutical drug delivery and wound applications, pressure sensitive adhesive products are manufactured, packaged and tested at the Healthcare Industries Materials Site utilizing principles of GMP guidelines for Active Pharmaceutical Ingredients (APIs).

Description	Typical Applications	Regulatory Status: FDA Material Application File	Regulatory Status: European Technical[1] and FDA Drug Master File	Biocompatibility Tests: Cytotoxicity	Biocompatibility Tests: Mutagenicity/Genotoxicity	Biocompatibility Tests: Skin Irritation	Biocompatibility Tests: Skin Sensitization	Biocompatibility Tests: Pyrogenicity (USP)	Biocompatibility Tests: Systemic Toxicity
Pressure Sensitive Adhesives									
Solvent-based non-sensitizing, non-irritating, pressure-sensitive adhesive formulations	• Adhesion of dressings, prosthetics and other devices to the body								
Dow Corning® MD7-4502 Silicone Adhesive		•	•	•	•	•	•		
Dow Corning® MD7-4602 Silicone Adhesive		•	•	•	•	•	•		
Customizable Pressure Sensitive Adhesives for Transdermal Delivery Systems[2]									
Amine-compatible adhesive in solvent; custom formulation upon solvent selection	• Skin adhesion of transdermal drug delivery systems; specifically designed for compatibility with aminofunctional drugs								
BIO-PSA® 430X Silicone Adhesive		•	•	•	•	•	•		•
BIO-PSA® 420X Silicone Adhesive		•	•	•	•	•	•		•
BIO-PSA® 410X Silicone Adhesive		•	•	•	•	•	•		•
Custom adhesive formulations in solvent	• Skin adhesion of transdermal drug delivery systems to the body								
BIO-PSA® 460X Silicone Adhesive		•	•	•	•	•	•		•
BIO-PSA® 450X Silicone Adhesive		•	•	•	•	•	•		•
BIO-PSA® 440X Silicone Adhesive		•	•	•	•	•	•		•
Solventless adhesive formulation with adjustable tack (customizable)	• Skin adhesion of transdermal drug delivery systems to the body								
BIO-PSA® Hot Melt Adhesive		•		•	•				•

Description	Typical Applications	Biocompatibility Tests[3]: Cytotoxicity	Biocompatibility Tests[3]: Skin Irritation	Biocompatibility Tests[3]: Skin Sensitization
Soft Skin Adhesive				
Two-part, platinum-catalyzed adhesive, unfilled silicone elastomer	• Clear and soft skin adhesive for wound dressing and pharmaceutical topical or transdermal applications			
Dow Corning® 7-9800 A & B		•	•	•

[1] Dow Corning can provide Technical Files as needed to meet requirements.

[2] X = 1 for heptane, X = 2 for ethyl acetate.

[3] Tested according to ISO 10993-1 standard for skin contact duration ≤30 days.

Typical Properties**

	Solids Content	Shear	Peel Adhesion	Tack	Solvent	Melt Viscosity at 185°C (365°F)	Solution Viscosity at 25°C (77°F)				
	Rheology – Eta* at 0.01 rad/s at 30°C (86°F)	mPa·s	mPa·s			g/cm	kg/6.25cm²	%
MD7-4502	5×10^7	2500		Ethyl Acetate	Medium	700	16	65
MD7-4602	5×10^6	3000		Ethyl Acetate	High	500	15	60
BIO-PSA® 430X	5×10^6	500[4], 1200[5]		Heptane	High	700	14	60
BIO-PSA® 420X	1×10^8	450[4], 800[5]		or	Medium	900	17	60
BIO-PSA® 410X	1×10^9	150[4], 350[5]		Ethyl Acetate	Low			60
BIO-PSA® 460X	5×10^6	1000[4], 2600[5]		Heptane	High	500	15	60
BIO-PSA® 450X	5×10^7	700[4], 1500[5]		or	Medium	700	16	60
BIO-PSA® 440X	5×10^8	450[4], 650[5]		Ethyl Acetate	Low			60
BIO-PSA® Hot Melt	5×10^5		25,000	None	Very High	300	11	100

	As Supplied** – Pot Life[6] at Room Temperature / Viscosity at 25°C (77°F)			After Curing** – Penetration (62.5 g probe weight) / Appearance	
	mPa·s	min.			mm/10
7-9800 A & B	400	140	Test Conditions: 60 min. at 140°C (284°F) then cooled to room temperature	Clear	95

** Specifications Writers: These values are not intended for use in preparing specifications. Please contact your local Dow Corning sales office prior to writing specifications on these products.

[4] 60% PSA solids in heptane.

[5] 60% PSA solids in ethyl acetate.

[6] Time from initial mixing to double viscosity.